SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

A Sphenoidal Ectopic Pituitary Adenoma as a Differential Diagnosis of Chordoma

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DOI: 10.36347/sasjm.2021.v07i11.010 | **Received:** 07.09.2021 | **Accepted:** 21.10.2021 | **Published:** 30.11.2021

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Abstract **Case Report**

Pituitary adenomas emerge from the adenohypophysis and are confined to the region of the sella turcica, however, other sites may be involved as a result of extension infiltration, or ectopic location, the ectopic involvement of the sphenoid is rare. Our case illustrated a woman patient with an ectopic invasive macroprolactinoma diagnosed as a chordoma of the skull base. In Our case, the first histological examination was consistent with a coincidental Intrasellar Chordoma and Pituitary adenoma, Immunostaining was positive for synaptophysin and prolactin with a Ki-67 index of 7%, suggestive of an invasive prolactinoma, in addition to the existence of vacuolated cells with foamy Cytoplasm resembling to hysaliphorous cells suggested the diagnosis of chordoma. However, immunohistochemical study using brachyury and S-100 protein have shown a negative stain. Thus, the diagnosis of chordoma was excluded. Thus, it is particularly important to maintain ectopic pituitary adenomas in sphenoidal or clival locations as the main differential diagnosis of chordoma; because the diagnosis can have significant implications on the management of the tumor, and can give us a golden opportunity for more conservative management (in our example managed with dopamine agonists), if the diagnosis can be made preoperatively rather than retrospectively based on histology.

Keywords: Ectopic, pituitary adenoma, chordoma, diagnosis, dilemma.

INTRODUCTION

Pituitary adenomas are common tumors that account for about 10% of intracranial neoplasms; most adenomas emerge from the adenohypophysis and are confined to the region of the sella turcica, and however other sites may be involved as a result of extension, infiltration, or ectopic location. Ectopic involvement of the sphenoid is rare.

Chordomas are uncommon malignant tumors of the axial skeleton that account for 1% of intracranial tumors and 4% of all primary bone tumors. They originate from embryonic remnants of the primitive notochord, since chordomas arise in bone; they are usually extradural and result in local bone destruction. They are locally aggressive but uncommonly metastasize.

Our case illustrated a woman patient with an ectopic invasive macroprolactinoma diagnosed as a chordoma of the skull base.

CASE REPORT

A 43-year-old woman with amenorrhea and galactorrhea for about 3 years consulted a gynecologist who advised her to take cabergoline 1 cp per week.

One year later, the patient had a nasal obstruction on her right side and had consulted a rhino laryngologist, nasofibroscppy found thickening of the cavum, and the histological examination of the biopsy was inconclusive, a facial MRI (magnetic resonance imaging), which was proposed which revealed an enhancing lesion measuring 52 × 40 × 38 mm that involved the entire clivus, sphenoidal sinus, extended laterally to the cavernous sinuses with extension into the sella turcica, and lower in the nasal cavity[figure 1].

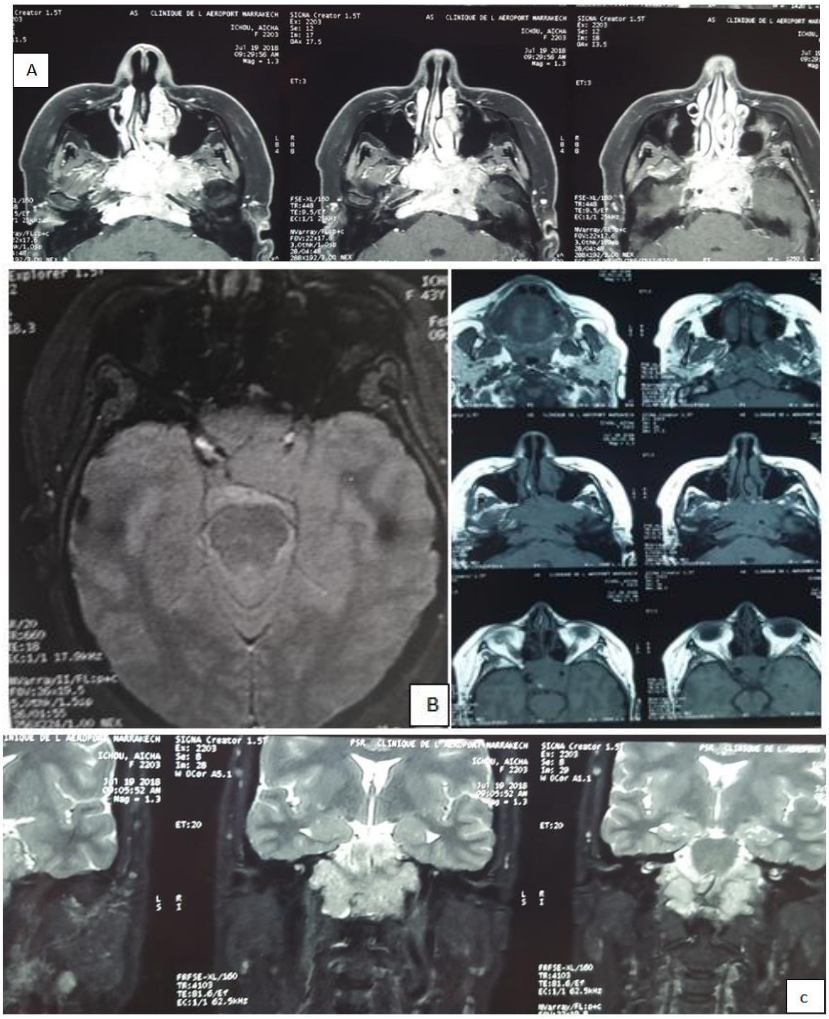


Fig-1: Preoperative magnetic resonance imaging with contrast, axial (a, b), and sagittal (c) sections, demonstrating contrast enhancing clivaltumor

And the patient was addressed to our department of endocrinology; the patient's medical history doesn't find other signs of insuffiance or hyper secretion of adenohypophysis, no polyuria polydipsia syndrome.

The patient reported no neurological complaints, no decreased visual acuity, and there were no noteworthy findings on physical examination.

Her complete biological assessment found high prolactin level = 4700 ng/ml passed to 123,5 after precipitation and elimination of bigtumotrbig prolactin [Table 1].

Table-1: Patients'sendocrinologicallabvalues

Free T4 (pmol/L)	11,5	12–22
TSH (mIU/L)	2.61	0.27–4.2
Prolactin(ng/mL)	4700	4,8–23.1
FSH (lU/L)	1,4	9–16.0 (women)
LH (lU/L)	0.1	10,2–15.0 (women)
Cortisol (μg/L)	123,7	62–194

T4=thyroxinehormone.
TSH=thyroid stimulating hormone.
FSH=follicle stimulating hormone.
LH=luteinizinghormone.

The case was discussed at an interdisciplinary brain tumor meeting and, ultimately, the patient was advised to undergo surgical resection via an endoscopic endonasal approach, intraoperatively, the lesion was friable and bleeding on contact, accordingly, a decision was made perioperatively to proceed with only macroscopic exerese and multiples biopsies.

Histopathological findings confirmed an epithelial neoplasm demonstrated as a pituitary adenoma, according to the endocrine architecture; the cells are provided with a strongly nucleoli round the nucleus, and the cytoplasm is abundant and eosinophilic, Immunohistochemical stains were positive for synaptophysin and prolactin, with a Ki-67 index = 7%, suggestive of a prolactin-secreting pituitary adenoma. Additional immunohistochemical stains seen in chordomas (EMA, S100, and Brachyury) were negative.

The patient started a dopaminergic agonist (cabergoline) and was followed up regularly by prolactin control and pituitary MRI.

DISCUSSION

The differential diagnosis of a clival tumor includes chordomas, most commonly (40%), meningioma, chondrosarcoma, astrocytoma, craniopharyngioma, germ cell tumors, non-Hodgkin's lymphoma, melanoma, metastatic carcinoma, and rarely ectopic pituitary adenoma [1].

Ectopic pituitary adenomas are thought to arise from residual cells along the migration tract of the pharyngeal pituitary as it travels from Rathke's pouch to the sella turcica, like pituitary adenomas [2], ectopic tissue can be categorized by size as either a macroadenoma (>1cm) or microadenoma (<1cm), The tumor can be further classified as functional or non functional based on whether or not the cell type is hormone-secreting [3,16].

Chordomas are slow-growing malignant bone tumors and are thought to arise from notochordal cell rests. Their incidence is rare, and they represent approximately 1% of all malignant bone tumors and 0.2% of intracranial tumors [4] Their location is usually related to the midline, and approximately 50% develop in the sacrococcygeal region, while 35% develop in the sphenooccipital region and 15% in vertebrae[5-7].

Pituitary adenomas often classically present with bitemporal hemianopsia, but ectopic adenomas typically do npit1ot unless they happen to involve the optic chiasm[10, 11 17] but these findings cannot distinguish a pituitary adenoma from other lesions such as a chordoma ; Fortunately the majority of ectopic adenomas are functional permitting a possible preoperative diagnosis based on history, physical exam, and basic labs alone (such in our case, the patient presented galactorrhea with amenorrhea, and elevated prolactin level which let us think about a prolactinoma), However cases of Chordoma with increased prolactin levels (pseudoprolactinoma) were reported [5,12].

On CT and MRI, the chordomas of the skull base are usually found to have a lobulated, "honeycomb" appearance, that may extend posteriorly to the prepontine cisterns, circles of Willis, cavernous sinuses, brain stem, and cause bone erosion, sellar and suprasellar chordomas may mimic pituitary adenoma, but are usually differentiated by the presence of calcification and / or bony destruction [13-15]. Intraoperative findings can also help to make differences [Figure 2].

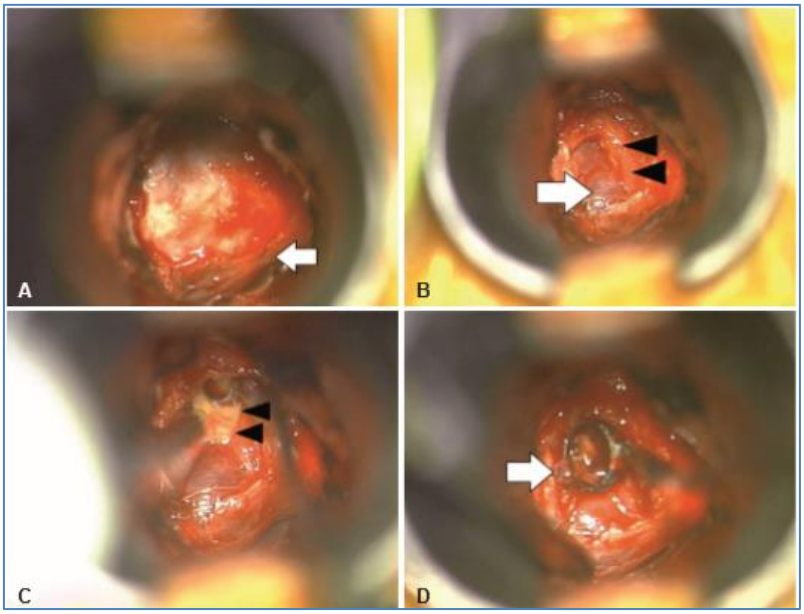


Fig-2: Intraoperative findings showing two different tumors. A: The intact dura and remnant bony sella (arrow). B: A yellowish and friable tumor located to the left and anterior side (arrowheads) and a cystic tumor located to the right side (arrow). C: A prominent yellowish and friable tumor (arrowhead). D: A mucoid substance in the cystic tumor (arrow) [3, 19].

Histologically, pituitary adenomas appear as a monomorphic expansion of usually one cell type with Lack of reticulin network among neoplastic cells. The growth pattern can be diffuse, trabecular, pseudo-acinar or pseudo-papillary. Most adenomas show uniform nuclear morphology, stippled chromatin and inconspicuous nucleoli with moderately abundant cytoplasm. Cytoplasmic Appearance usually correlates with the content of hormone-containing secretory cells. lmmunohistochemical staining allows for the classification of pituitary adenomas according to their Hormone content [9].

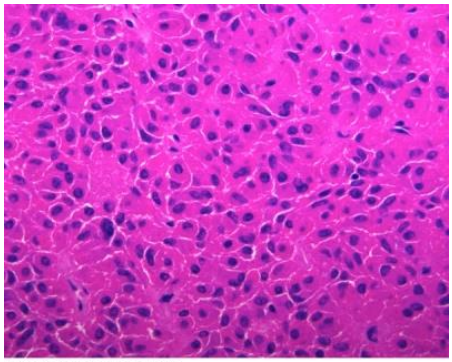
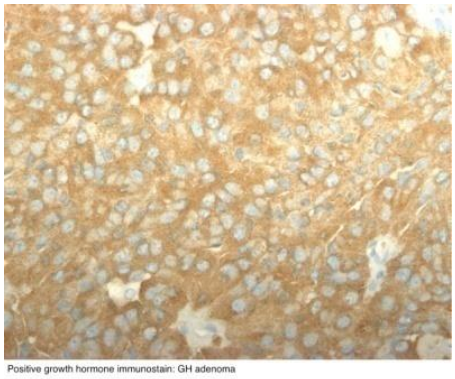
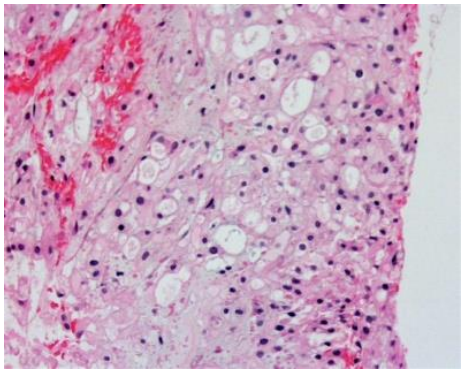
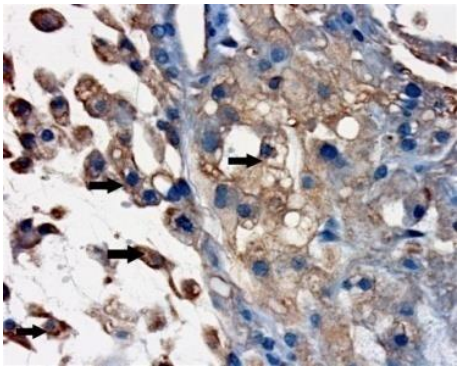
Microscopically, chordomas show cells with abundant clear to eosinophilic cytoplasm that may have A vacuolated appearance (physaliphorous cells) set in

an abundant mucoid matrix cell. Arranged in lobules are embedded. Physalipourous cells are usually immunoreactive for EMA, S-100 protein, Pan-keratin and brachyrury, which is highly specific and may distinguish chordoma from histological mimics include chondrosarcoma, chordoid meningioma, and pituitary adenoma [10,11]. [Figure 3].

In our case, in addition to the location, the existence of an area of vacuolated cells with foamy Cytoplasm resembling to hysaliphorous cells suggested the diagnosis of chordoma. The Immunohistochemical studies using brachyury and S-100 protein has shown a negative stain. Thus the diagnosis of chordoma was excluded.

Here is a table summarizing the histological characteristics allowing to differentiate between pituitary adenoma and chordoma [Table 2].

Table-2: Summary of the characteristics of pituitary adenomas and chordomas

	Pituitary adenoma	**Chordoma**
Microscopic description	-- Most adenomas show moderately abundant cytoplasm with a uniform nuclear morphology, stippled chromatin, and inconspicuous nucleoli -- Cytoplasmic appearance usually correlates with a content of hormone-containing secretory cells.	-- Cords and lobules of physaliferous (having bubbles or vacuoles) cells separated by fibrous septa with extensive myxoid stroma -- Cells may be very large, with vacuolated cytoplasm and prominent vesicular nucleus
Microscopic images	 Densely granulated adenoma 40x  Positive growth hormone immunostain: GH adenoma	  **Synaptophysin**
Positive stains	--- **synaptophysin** --- Routine hormone stains include prolactin, ACTH, GH, TSH, LH, FSH and alpha subunit --- **Reticulin** (useful in identifying normal acinar architecture versus distorted and fragmented staining pattern in adenomas) --- **Ki67** (often used proliferative indices Specific transcription factors: SF1, PIT-1stains or T-PIT)	---**S100**, --- **keratin** (**CK8** / **18**, **CK19**, **AE1** / **AE3**), --- **EMA**, --- **5' nucleotidase**, ---**CEA, lysozyme** --- **Brachyury** (may distinguish chordoma from histologic mimics, including clear cell renal cell carcinoma, chondrosarcoma, chordoid meningioma).
Negative stain,	GFAP, CK7, CK20, TTF1,	CK7, CK20, chromogranin
Electron microscopy description	Acidophil stem cell adenomas show numerous enlarged mitochondria with, loss of cristae and presence of electron dense tubular structures	Mitochondria - endoplasmic reticulum complexes, parallel bundles of crisscrossing tubules and desmosomes

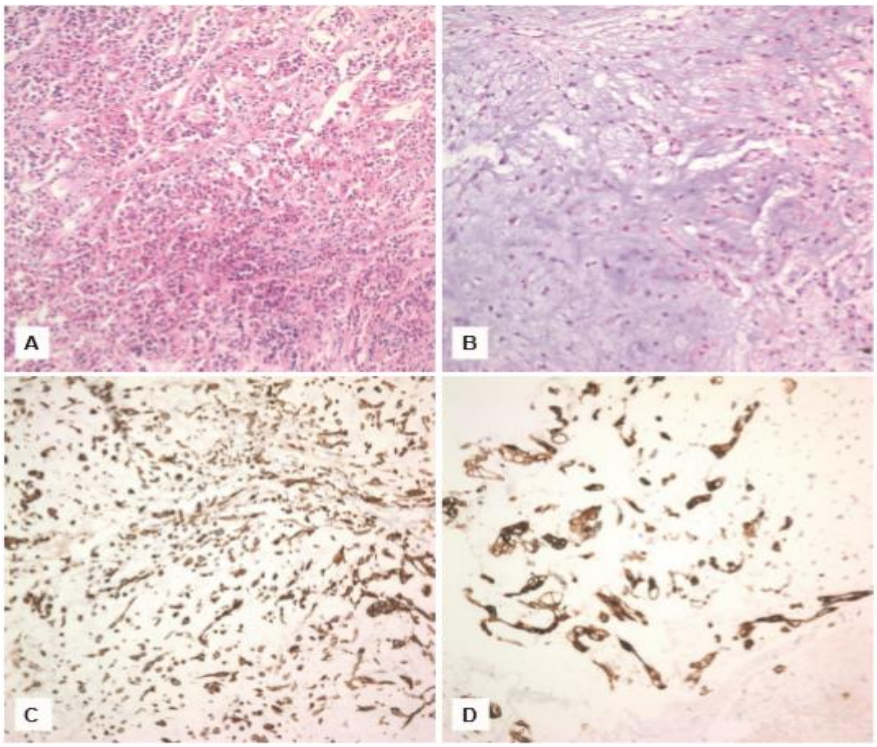


Fig-3: Histopathological findings of two different tumors. A: Pituitary adenoma: the tumor cells consist of small, oval or polyhedral cells. They are arranged in a cord or acinar pattern. The nuclei of tumor cells are round or oval and contain stippled chromatin (H&E, ×200). B: Chordoma: the neoplasm consists of strands of cells with vacuolated cytoplasm (physaliphorous cells) (H&E, ×200). The neoplastic cells of the chordoma are reactive with (C) cytokeratin-20 and (D) epithelial membrane antigen antibodies in the cytoplasm and cell membrane (×200). H&E, hematoxylin and eosin [4, 18]

It is particularly important to maintain ectopic pituitary adenomas in sphenoidal or clival locations as the main differential diagnosis of chordoma; because the diagnosis can have significant implications on the management of the tumor, and can give us a golden opportunity for more conservative management (in our example managed with dopamine agonists), if the diagnosis can be made preoperatively rather than retrospectively based on histology.

The review of the literature shows

- A case of a chordoma presenting with increased prolactin level"Pseudoprolactinoma"taken as a pituitary adenoma and was medically treated with bromocriptin, then in view of the persistence of the tumoral process, the patient has benefited from surgical treatment and the diagnosis of chordoma was made late on histological examination at the metastatic stage with neurological sequelae[1].
- We report also at the opposite case of an ectopic adenoma confused as a chordoma in a 41 -years-old man with an incidental clival lesion, originally presumed to be a chordoma and the histological diagnosis was about a prolactinoma, after a more focused history following the postoperative diagnosis of prolactinoma, it was discovered retrospectively that the patient had a significant drop in libido throughout the previous 7-8 years [2], However in our case the diagnosis of prolactinoma was earlier because our patient is a woman with amenorrhea and galactoctorea, contrariwise men in general do not consult for erectile dysfunction and problems of libido which delays the starting of dopamine agonists.
- Finally, it should be noted that cases of Coincidental Intrasellar Chordoma and Pituitary Adenoma were described; a 68-year-old female presented partial abducens nerve palsy in the right eye due to the intrasellar cystic tumor. After endonasal trans-sphenoidal surgery, intraoperative and histopathological findings confirmed the co-occurrence of an entirely intrasellar chordoma and pituitary adenoma [3].

CONCLUSION

A large tumor in the clivus in the appropriate clinical setting often leads to the presumptive diagnosis of chordoma, radiollogically the diagnosis of chordoma is suggested by accompanying destruction of the skull base, however, clinical findings and radiographic features overlap among the various types of skull base tumors and the definitive diagnosis often requires histological examination.

Pituitary adenomas that are large and destroy the clivus may present a diagnosis dilemma because they are relatively unusual in that location and may imitate other tumors; the absence of tumor necrosis is a key observation that should raise the possibility of an invasive pituitary adenoma.

Conflict of Interests

The authors declare that they have no conflict of interests.

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